

uc3m



Machine learning vs. knowledge based approaches to ADR identification

November 2017



Topics

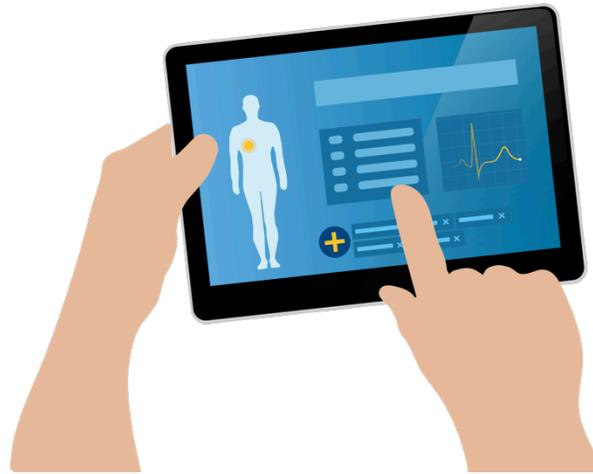
- . Short about us
- . Identifying ADRs
- . Machine Learning for semantic relations identification
- . Results
- . Challenges

SHORT ABOUT US

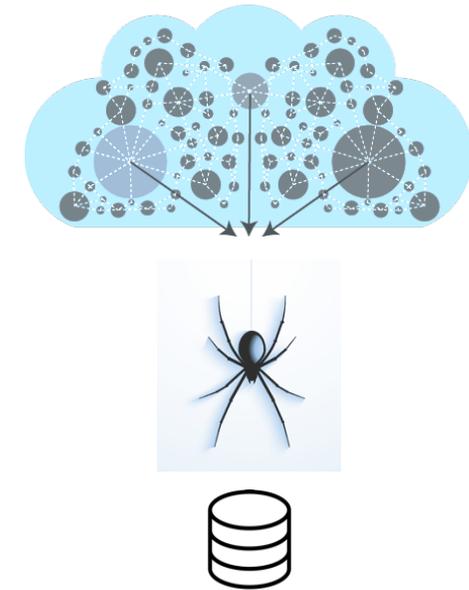
Focus on text-analytics for Pharmaceuticals. Since 1998



Voice of the Patient



Electronic Health Records



Other text sources

Scientific literature – FDA –
Patents – Business opportunities

SHORT ABOUT US

Advanced Databases Group, Universidad Carlos III de Madrid

- Research lines:
 - Natural language processing
 - Accessibility
- Resources produced:
 - ***Drug-drug-interaction collection (DDI Corpus)***
 - ***DINTO ontology***

The logo for Universidad Carlos III de Madrid (uc3m) is displayed in a bold, blue, sans-serif font.

Our goal at TAC ADR

“

Combine Knowledge Based with Machine Learning
Based approaches to leverage ADR identification”

Identifying ADRs

TOPIC EXTRACTION

NLP and Resource based approach

◦ SIDER

◦ UMLS

◦ Training corpus

Elements ?

- Entries
- Ontology
- Settings

Actions

[Build](#) [Delete](#)

[Import](#) [Export](#)

[Test](#)

Do you need more information? Check out the [documentation](#), or just drop us a line through our [support](#) form.

Entries ?

Show **10** entries Search:

Actions	ID	Form	Type	Ontology Type	Last updated
✎ 🗑	59c92278ba02d	"penile "popping" sound"	ENTITY	AdverseReaction	2017-09-25 17:36:24
✎ 🗑	59c9228a27fc7	1st degree heart block	ENTITY	AdverseReaction	2017-09-25 17:36:42
✎ 🗑	59c9228b00efd	2nd degree heart block	ENTITY	AdverseReaction	2017-09-25 17:36:42
✎ 🗑	59c9248d2cd5f	5'nucleotidase increased	ENTITY	AdverseReaction	2017-09-25 17:45:17
✎ 🗑	59c9247da8b7c	A-hypervitaminosis	ENTITY	AdverseReaction	2017-09-25 17:45:01
✎ 🗑	59c923b661f2f	A-V dissociation	ENTITY	AdverseReaction	2017-09-25 17:41:42
✎ 🗑	59c922a13f4d5	A.R.D.S.	ENTITY	AdverseReaction	2017-09-25 17:37:05
✎ 🗑	59c92479057bb	AAION	ENTITY	AdverseReaction	2017-09-25 17:44:57
✎ 🗑	59c9247909336	AAION	ENTITY	AdverseReaction	2017-09-25 17:44:57
✎ 🗑	59c92484e3ed0	Abasia	ENTITY	AdverseReaction	2017-09-25 17:45:08

(21826 entries) Previous [1](#) [2](#) [3](#) [4](#) [5](#) ... [2183](#) Next

[+ Add new entry](#)

TOPIC EXTRACTION

NLP and Resource based approach

◦ SIDER

◦ UMLS

◦ Training corpus

sementity:

class: instance
type: Top>AdverseReaction
meddra_ilt: AAION
meddra_ilt_id: 10068247
meddra_pt: Optic ischaemic neuropathy
meddra_pt_id: 10030924
cui_id: C2242711
meddracui_id: C0155305
source: SIDER

sementity:

class: instance
type: Top>AdverseReaction
meddra_ilt: AAION
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meddra_pt: Arteritic anterior ischaemic optic neuropathy
meddra_pt_id: 10030924
cui_id: C2242711
meddracui_id: C2242711
source: SIDER

Dictionary	#entries
Adverse Reactions	21,826
Factor	41
Severity	158
Animal	27
DrugClass	101

TOPIC EXTRACTION
NLP and Resource based approach

- And some rules to identify negation:

```
<<without|exclude|decrease|reduce>> :-  
ENTITY {"type":"NegationLeft", "label":"$1"}  
+ CONSUME {}  
<<{AFFECTEDADR}>> :-  
ENTITY {"type":"AffectedAdr", "label":"$1"}  
  
“...without associated bleeding events. ...”
```

- MeaningCloud Insights Engine API supports this rule syntax

**Machine Learning
for semantic
relations
identification**

Machine learning for semantic relations identification

Representing ADR mention context through a set of features:

- M1TXT, M2TXT, BWTXT: the text of both/between mentions.
- C1BOW, C2BOW: bag-of-words of both mentions.
- C1POS, C2POS: part of speech of both mentions.
- PB1POS, PA1POS, PB2POS, PA2POS, PWPOS: the PoS tags of the two tokens before/after/between both mentions.
- WA1TXT, WB2TXT, WA2TXT, WB1TXT: the two tokens after/before the mention.
- LA1LEM, LB2LEM, LA2LEM, LB1LEM: the lemmas of the two tokens after/before both mentions.
- LWLEM: the lemmas between of the two mentions
- NTOKB: the number of tokens between the two mentions.

ADRMention – Other pairs (where Other is Severity, DrugClass, Negation, Animal or Factor)

Machine learning for semantic relations identification

And the algorithm?

- SVM, support vector machines (using scikit-learn on Python)
- Specifically, SVC implementation:
 - Default parameter values
 - Linear kernel

But, no deep learning??!!

Of course (CNN), but not in the official runs.

Results

Results

- Task 1. ADR and related entities

Type	P	R	F1
Exact (+type)	54.79	66.33	60.01
Exact (-type)	55.78	66.34	60.60

Table 3: Task 1 results on the test set.

Type	P	R	F1
AdverseReaction	63.82	70.77	67.12
Severity	37.13	49.52	42.44
Factor	4.05	7.65	5.3
Negation	10.59	53.76	17.7
DrugClass	19.23	39.63	25.9
Animal	76.56	56.98	65.33
Macro	54.79	66.33	60.01

Low precision!!

Table 4: Task 1 results by type of mention on the test set.

- Task 2. Relations between ADRs and entities

Type of Relation	P	R	F1
Negated	8.43	4.86	6.17
Hypothetical	5.95	9.56	7.34
Effect	24.94	25.74	25.33
Macro	12.19	15.59	13.68

Table 5: Task 2 results on the test set.

Type of Relation	P	R	F1
Negated	1.12	27.59	2.15
Hypothetical	35.5	52.49	42.36
Effect	24.93	48.77	32.99
Macro	46.7	49.97	47.32

Oh, oh!!

Table 6: Task 2 results using correct mentions on the test set.

Results

- Task 3. Positive ADRs

	P	R	F1
Micro	70.03	71.42	70.71
Macro	69.23	72.93	70.13

Table 7: Task 3 results on the test set.

*Pretty good!!
Only a few negated mentions?*

- Task 4. Normalization through MedDRA

	P	R	F1
Micro	73.40	80.25	76.67
Macro	72.10	80.38	75.29

Table 8: Task 4 results on the test set.

*Using dictionaries with
semantic information
produces nice results*

Challenges

Challenges

- Negation identification requires more effort (not only on the ADRs field).
Some weird things found in the test set:

Eg.: The most frequently observed malignancies other than non-melanoma skin cancer ...

Negation?

- CNNs and the use of syntactic features improves results

	P	R	F1
Other	0.71	0.81	0.76
Negated	0.72	0.40	0.51
Hypothetical	0.75	0.75	0.75
Effect	0.76	0.61	0.68
Avg / total	0.73	0.73	0.73

Challenges

- Recall must be improved:
 - separated multiword mentions
 - ADRs with no MedDRA code, enough lexical resources?
- How to approach errors when applying deep learning?
- Enough accuracy for practical applications? What does FDA think?

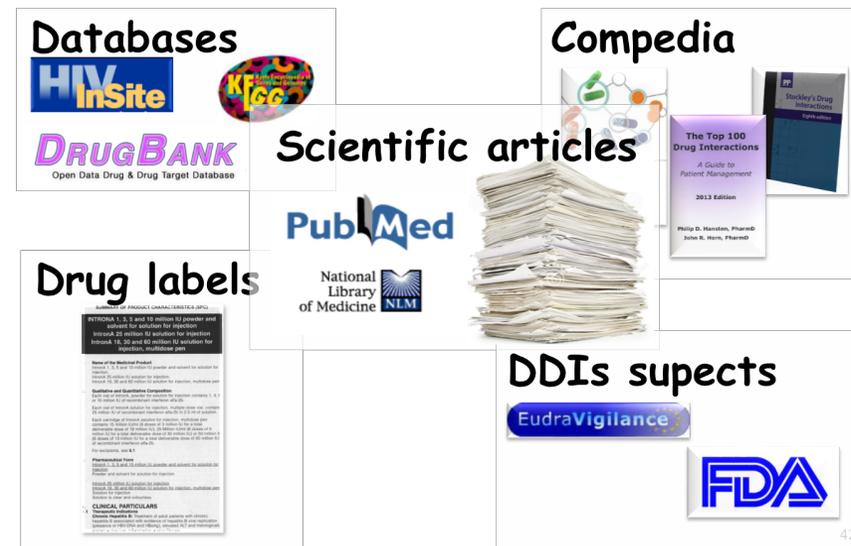
Thanks

QUESTIONS?

LabDA Resources

Corpus DDI (Drug-Drug Interactions)

- ▶ 1,025 annotated documents, 18,502 entities and 5,028 DDIs (by expert pharma)
- ▶ MedLine and DrugBank texts
- ▶ Annotations guidelines and interannotator agreement.
- ▶ Available at labda.inf.uc3m.es
- ▶ Used at DDIExtraction 2011 and DDIExtraction 2013 Semeval Tasks



/ddi2013/DrugBank/DrugBank_d59

stav

1 The effects of **ERGOMAR** may be potentiated by **triacetyloleandomycin** which inhibits the metabolism of **ergotamine**. The pressor effects of **ERGOMAR** and other **vasoconstrictor drugs** can combine to cause dangerous hypertension.

LabDA Resources

DINTO Ontology- knowledge about drugs and interactions (11,555 DDIs and 8,786 pharmacological entities). Available at [OBO Foundry](#)



Application to Information Extraction and Prediction

The screenshot displays the 'The Drug-Drug Interactions Ontology' web interface. The main title is 'The Drug-Drug Interactions Ontology' with sub-navigation links: Summary, Classes, Properties, Notes, Mappings, and Widgets. A 'Jump To:' search box is present. The left sidebar shows a hierarchical tree of classes, with 'chemical entity' selected. The right pane shows the 'Details' tab for the 'chemical entity' class, including its preferred name, ID, definition, label, prefixIRI, prefLabel, subClassOf, and disjointWith relationships.

Property	Value
Preferred Name	chemical entity
ID	http://purl.obolibrary.org/obo/CHEBI_24431
Definition	A chemical entity is a physical entity of interest in chemistry including molecular entities, parts thereof, and chemical substances.
label	chemical entity
prefixIRI	obo2:CHEBI_24431
prefLabel	chemical entity
subClassOf	Thing
disjointWith	study subject role drug interaction pharmacokinetic parameter DDI mechanism pharmacokinetic process



MeaningCloud LLC

Automating the extraction of Meaning from any information source.

 Address
35-37 36th Street
11106 Astoria NY

 Contact Info
jmartinez@meaningcloud.com

 Telephone
Phone: +1 (646) 403-3104



meaningcloud.com